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What's in this issue?

Calcium Absorption and Proton Pump Inhibitors

By Catherine Dejongh

Is there a risk of poor calcium absorption when taking a proton pump inhibitor? Proton pump inhibitors are routinely used for various gastrointestinal (GI) disorders, including gastroesophageal reflux disease. Often a proton pump inhibitor like Prilosec®, Prevacid®, Nexium®, or Protonix® is used for the elderly who have GI disorders. Often these individuals may also be receiving calcium products to prevent osteoporosis; so naturally, one must be alert to the possibility of drug interactions.

One study has been done to determine whether calcium absorption was affected by use of omeprazole, a proton pump inhibitor. Calcium absorption was decreased by an average of 41% for the 18 participants who completed the study. There was one outlier, and if that data is discarded, calcium absorption was decreased by an average of 61%±32%. This study looked at elderly women under fasting conditions. Bearing in mind that the sample population for this study was very small, findings may indicate a drug interaction between calcium carbonate and omeprazole.

Calcium absorption is dependent on many factors, including calcium type and dose, diet, and age. For those individuals who are on calcium and a proton pump inhibitor, it makes sense to evaluate the need for the proton pump inhibitor. If the proton pump inhibitor is still needed, monitoring and adjustments of calcium levels may be warranted. Future studies are needed, however, to evaluate whether the decreased absorption is significant for long-term outcomes such as fracture rates.

O'Connell MB, Madden DM, Murray AM, Heaney RP, Kerzner LJ. Effects of proton pump inhibitors on calcium carbonate absorption in women: a randomized crossover trial. Am J Med 2005;118:778-781.

New Drugs

Daytrana (methylphenidate)	transdermal patch for the treatment of ADHD
Emsam (selegiline)	transdermal patch for the treatment of depression
Vivitrol (naltrexone)	once monthly injectable formulation for the treatment of alcohol dependence

Consultant Corner **By Catherine Dejongh**

1) **What is the risk of osteoporosis and osteomalacia with use of anticonvulsants?**

Anticonvulsants can impact bone metabolism by causing osteomalacia and/or osteoporosis. Some anticonvulants increase vitamin D breakdown by activating liver enzymes. This leads to vitamin D deficiency, which leads to osteomalacia. Osteomalacia is a condition where there is a lack of calcium in the bone matrix and an increase in the un-mineralized bone matrix. Osteoporosis occurs when both the calcium matrix and un-mineralized bone matrix are decreased.

Osteoporosis, stemming from anticonvulsant use, is most likely the result of decreased calcium absorption and increased breakdown of sex steroids. The anticonvulsants most commonly known for effecting bone mineral are carbamazepine, oxcarbazepine, phenytoin, and phenobarbital. The drugs that are known not to effect bone include; lamotrigine, topiramate, valproate, and gabapentin.

In order to prevent loss of bone material, it is important to provide calcium and Vitamin D supplements to patients on anticonvulsants, especially the elderly and institutionalized. The use of medications designed for osteoporosis, like Fosamax and Evista, can also be used for secondary prophylaxis for those individuals with decreased bone mineral density and other risk factors.

Vestergaard P. Epilepsy, osteoporosis and fracture risk – a meta-analysis. *Acta Neurol Scand* 2005;112:277-286.

2) **Estrogen for hypersexuality: Standard of practice and ethical considerations.**

Choice of treatment for hypersexuality depends on the patient's situation, behaviors, medication regimen, and any underlying medical conditions. Medication interventions for hypersexuality in nursing home patients, particularly males, should be reserved for those patients where nonpharmacologic interventions fail.

Medications helpful in controlling these behaviors include selective serotonin reuptake inhibitors (SSRIs), antipsychotics, and hormonal agents. In the case of hypersexuality as a behavior issue, medications found beneficial in case reports were trazodone, estrogen, and leuprolide acetate.

There are ethical issues to consider. Treatment regimens can be seen as hindering sexual expression and violating an individual's rights. However, not treating the condition places facility staff and other residents at risk for mental and physical trauma.

Black B, Muralee S, Tampi RR. Inappropriate sexual behaviors in dementia. *J Geriatr Psychiatry Neurol* 2005;18:155-162.

3) **Lamictal use in the elderly.**

Lamictal (lamotrigine) is a newer antiepileptic medication that is FDA approved for partial seizures, bipolar type 1, and Lennox-Gastaut syndrome. The medical treatment of epilepsy has changed in recent years due to the development of these newer antiepileptic medications. The new medications are viewed as more suitable for the elderly than phenytoin, due to the more favorable properties like decreased adverse effects. Also, lamotrigine does not require as much care in dose adjustments and has fewer adverse cognitive effects.

Pugh MJV, Cramer J, Knoefel J, et al. Potentially inappropriate antiepileptic drugs for elderly patients with epilepsy. J Am Geriatr Soc 2004; 52:417-422.

4) **Lamictal and antipsychotics used for bipolar disorder.**

Bipolar disorder is a serious mental illness affecting many people. The gold standard of long term treatment is lithium, because it protects against both manic and depressive relapses. However, if lithium is ineffective, valproate or atypical antipsychotics have been recommended. These treatments are better at repressing manic episodes than depressive relapses. The atypical antipsychotics are all approved for the acute treatment of a manic episode. Olanzapine and aripiprazole are approved for maintenance therapy. Lamotrigine is a long-term treatment option that protects more against depressive than manic episodes.

McAllister-Williams RH. Relapse prevention in bipolar disorder: a critical review of current guidelines. Journal of Psychopharmacology 2006; 20:12-16.

Simons WR, Krishman AA. The economic value of lamotrigine as a mood stabilizer: a U.S. managed care perspective. Pharmacoeconomics 2004;44-49.

Marken PA, Pies RW. Emerging treatments for bipolar disorder: safety and adverse effect profiles. Ann Pharmacother 2006;40:276-285.

Focus Drug of the Quarter By Catherine Dejongh

Emsam® (Selegiline)

Emsam® is a monoamine oxidase inhibitor (MAOI) that is administered with a transdermal patch. Emsam® is indicated for the treatment of major depressive disorder. The transdermal route of administration allows Emsam® to bypass first-pass metabolism, which in turn, decreases the potential for food interactions and toxic tyramine levels accumulating in the body. The transdermal application also allows for Emsam® to reach higher levels in the brain than when given orally.

The Emsam® patches are available in three sizes; 6 mg, 9 mg, and 12 mg over a 24 hour period. The recommended starting and target dose is 6 mg/24 hours. Safety and efficacy data is not known for both the 9 mg/24 hour and 12 mg/24 hour doses. Dose increases should be made at minimum intervals of two weeks and in 3 mg/24 hour increments. Emsam® should be applied to dry, intact, hairless skin on the upper torso, upper thigh, or outer surface of the upper arm once every 24 hours.

The most common adverse effects of Emsam® are headache, dizziness, and diarrhea. It is also noted from studies that one-third of patients experienced application site reactions, with some needing topical corticosteroids.

The potential for drug interactions while using Emsam® is significant and should be closely monitored. Emsam® should not be used together with other antidepressants, e.g., SSRIs, TCAs, venlafaxine, or bupropion, some analgesics (meperidine, tramadol, methadone, or propoxyphene), dextromethorphan, St. John's Wort, mirtazepine, buspirone, or cyclobenzaprine. If other antidepressants are being used, or have recently been used, it is important to make sure that the antidepressant has been stopped for at least seven to fourteen days prior to starting Emsam. If patients are taking fluoxetine, the fluoxetine should be stopped for five weeks before starting Emsam. Patients should wait at least two weeks after stopping Emsam® to start any drug with a known interaction.

The potential for hypertensive crisis due to toxic tyramine levels is less with transdermal Emsam®. The use of some medications can increase this risk and should be avoided; e.g., phenylpropanolamine, some weight-loss drugs, and pseudoephedrine. Patients are not necessarily required to follow a tyramine restricted diet, but should be provided with a medication guide that includes a listing of foods containing tyramine. Patients on the 9 mg/24-hour and 12 mg/24-hour patches should follow tyramine restricted diets until further safety data is collected.

Due to safety concerns and drug interactions, Emsam® should only be used for patients who fail with other antidepressants or cannot tolerate other medications. The need to change patches everyday, application site reactions, and tyramine restricted diets may prove difficult for patients, and compliance may not be improved by transdermal application. Emsam® is safe for use in elderly patients. The recommended dose is 6 mg/24 hours. Emsam should be reserved for those situations where depression is intractable to other treatment modalities. Therefore Emsam will not be routinely seen in most environments.